

PABST PATENT **GROUP**



Pabst Patent Group LLP 400 Colony Square, Suité 1200 1201 Peachtree Street Atlanta, GA 30361

Telephone (404) 879-2150 Telefax (404) 879-2160

information@pabstpatent.com www.pabstpatent.com

TELEFAX

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To:

USPTO

Telephone:

Telefax: 703-872-9306

From: Patrea L. Pabst

Telephone: (404) 879-2151

Telefax: (404) 879-2160

Our Docket No. Your Docket No.

Client/Matter No. 078230/00031

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MESSAGE:

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

Philip John Burke and Richard John Knox

Serial No.: 10/099,830

Art Unit:

4061

Filed:

March 13, 2002

Examiner: G. Nickol.

For:

THERAPEUTIC SYSTEMS

EEE TRANSMITTAL			Complete if Known						
FEE TRANSMITTAL			Application Number 1			10/099,830			
for FY 2004			Filing Date			March 13, 2002			
		First Named Inventor			ntor Phili	Philip John Burke			
Effective 10/01/2003. Patent fees are subject to annual revision	-	Examiner Name			Gan	Gary B. Nickol			
Applicant claims small entity status. See 37 CFR 1.27						1642			
TOTAL AMOUNT OF PAYMENT (\$)						ERD 100 CON			
METHOD OF PAYMENT (check all that apply)	FEE CALCULATION (continued)								
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					Examiner action	on	•		
to the above-identified deposit account.	1805	1,840*	1805	1,840*	Requesting pu Examiner action		IR after		
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SUBMITTED BY (Complete (if applicable))									
Name (Print/Type) Patrea L. Pabst		Registrat Attorney/A		31	,284	Telephone	(404) 879-21	151	
Signature						Date	May 5, 2	2004	

Under the Pa	acenwork Reduction Act of 1995	no person:	U.S. Paten	t and Tradema	rk Officer 11 C	PTO/SB/21 (08-03) ugh 07/31/2006. OMB 0651-0031 DEPARTMENT OF COMMERCE days a velid OMB control number			
			Application Number	10/099,8					
TRANSMITTAL FORM (fo be used for all correspondence after initial filing)		Filing Date	March 1	3, 2002					
		First Named Inventor	Philip Jo						
		Art Unit	1642						
		İ	Examiner Name	Gary B.	Nickol				
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Firm			F APPLICANT, ATTORNE		ENT				
or Individual name Signature	Patrea L. Pabst, Esq., I 400 Colony Square, St			p LLP					
Date	May 5, 2004								
CERTIFICATE OF TRANSMISSION/MAILING									
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Signature		\bigvee			Date	May 5, 2004			

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THERAPEUTIC SYSTEMS

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

RESPONSE TO RESTRICTION REQUIREMENT

Sir:

Responsive to the Restriction Requirement mailed on April 5, 2004, please consider the following remarks. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

RESPONSE TO RESTRICTION REQUIREMENT

In the Claims

Claims 1-33 (Canceled).

34. (Currently amended) A therapeutic system comprising a prodrug which is converted to a substantially cytotoxic drug by the action of NQO2 and nicotinamide riboside (reduced) (NRH) or an analogue thereof which can pass reducing equivalents to NQO2 a compound of formula I

$$\mathbb{R}^2$$
 \mathbb{R}^3
 \mathbb{R}^3

wherein R¹ is selected from the group consisting of substituted alkyl, including substitution by CONH₂. OH, halogen, CN, and COOH; aryl; substituted aryl; CONR^aR^b, where R^a and R^b are independently H, alkyl, or substituted alkyl, and R² and R³ are independently H, alkyl, or substituted alkyl, halogen, CN, COOH, alkyl, or substituted alkyl and R⁴ is any of H, alkyl, substituted alkyl, halogen, CN, COOH, CONH₂, or OH, wherein the compound can pass reducing equivalents to NOO2, in a form for administration to a patient in need thereof.

Claims 35-40 (Canceled)

41. (Currently amended) The method-system of claim 29 34, wherein the analogue of NRH compound is 1-(carboxamidomethyl)-dihydronicotinamide.

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RESPONSE TO RESTRICTION REQUIREMENT

42. (New) The system of claim 34, wherein the compound has formula II

wherein R is a substituted alkyl, comprising one or more groups selected from the group consisting of CNH₂, OH, halogen, CN, and COOH.

- 44. (New) The system of claim 34, wherein the alkyl group is a C_1 to C_6 alkyl.
- 45. (New) The system of claim 34, wherein R is selected from the group consisting of -CH₂CONH₂, -CH₂CH₂CH₂COOH, and -CH₂CH₂COOH.
- 46. (New) The system of claim 34 wherein the analogue of NRH is 1-(carboxamidomethyl)-dihydronicotinamide.

Remarks

Restriction Requirement

In the Office Action mailed April 5, 2004, the claims were divided into fifteen (15) groups, as follows:

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RESPONSE TO RESTRICTION REQUIREMENT

Group I, claims 1-7 and 24, drawn to compound comprising a target cell-specific portion and human NAD(P)H:quinine reductase 2 (NOO2);

Group 2, claims 1-7, 12, and 24, drawn to a compound comprising a target cell-specific portion and a polynucleotide encoding NQO2, variant, fragment, fusion, or derivative;

Group 3, claims 8-11, drawn to a recombinant polymnucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2;

Group 4, claims 13-17, drawn to a therapeutic system comprising a protein compound comprising a target cell-specific portion and human NAD(P)H:quinine reductase 2 and a prodrug;

Group 5, claims 13-17, drawn to a therapeutic system comprising a polynucleotide encoding NQO2, a target cell-specific portion, and a prodrug;

Group 6, claims 18-23, drawn to a method of treating a patient with a target cell to be destroyed comprising administering a protein compound comprising a target cell-specific portion and human NAD(P)H:quinine reductase 2;

Group 7, claims 18-23, drawn to a method of treating a patient with a target cell to be destroyed comprising administering a recombinant polynucleotide, comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2;

Group 8, claims 25 and 26, drawn to use of a protein compound comprising a target cell-specific portion and human NAD(P)H:quinone reductase 2;

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RESPONSE TO RESTRICTION REQUIREMENT

Group 9, claims 25 and 26, drawn to use of a recombinant polynucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding NQO2;

Group 10, claims 29, 31-33, 40 and 41, drawn to a method of treating a human patient with a target cell to be destroyed comprising administering CB1954 and NRH or an analogue thereof;

Group 11, claim 34, drawn to a therapeutic system comprising a prodrug and nicotinamide riboside;

Group 12, claim 35, drawn to nicotinamide riboside (NRH) or an analogue thereof;

Group 13, claims 36 and 37 drawn to use of NRH in the manufacture of a medicament for treating a human patient with a target cell to be destroyed;

Group 14, claims 27, 28, and 38, drawn to use of a prodrug; and

Group 15, claim 39, drawn to a kit comprising a means for determining whether a target cell to be treated expresses NQO2 and NRH or an analogue thereof which can pass reducing equivalents to NQO2.

This application is a continuation of U.S.S.N. 09/445,865 filed February 11, 2000, now allowed. The parent application was subject to a restriction requirement on February 13, 2001. The same claims are presented in this application yet have been subjected to a different restriction requirement by the same examiner. On this basis alone, the undersigned must traverse the restriction requirement. For example, claims 13-17 were previously divided into three groups (this restriction was traversed) – now they are divided into two groups; claim 32

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RESPONSE TO RESTRICTION REQUIREMENT

was previously placed into group 12; now it is placed into group 10 with a different set of claims.

This makes it impossible to determine what the examiner believes the different inventions to be.

To the extent one can make an election, applicants elect to prosecute the invention of

claim 34, group 11.

Claims 1-33 and 35-40 have been canceled, without prejudice with the understanding that

these claims can be prosecuted in later filed applications. Claim 41 has been amended to depend

from claim 34, which as been amended to refer to a compound of formula I. New claims 42-46

have been added. Support for the new claims are found in the specification at least at page 49,

line 25 to page 50, line 7 and page 51, lines 7-8; page 50, line 12 to page 51, line 1; page 51, line

4; page 51, lines 10-22; and page 46, lines 7-9.

Election of Species

Groups 1 and 2 were further classified by species: a) an antibody or fragment or

derivative, and b) macromolecule. The election of species is moot since these claims have been

canceled.

No change in inventorship is required by virtue of the response to restriction requirement.

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U.S.S.N. 10/099,830 Filed: March 13, 2002 RESPONSE TO RESTRICTION REQUIREMENT

Issuance of an office action on the merits of claims 34 and 41, as amended, and new claims 42-46 is respectfully solicited.

Respectfully submitted,

Patrea L. Pabst Reg. No. 31,284

Date: May 5, 2004

PABST PATENT GROUP LLP 400 Colony Square, Suite 1200 1201 Peachtree Street Atlanta, Georgia 30361 (404) 879-2151 (404) 879-2160 (Fax)

Certificate of Facsimile Transmission

I hereby certify that this Response to Office Action, and any documents referred to as attached therein are being facsimile transmitted on this date, May 5, 2004, to the Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Patrea L. Pabst

Date: May 5, 2004

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